Relative Evaluation of Left Heart Bypass, Whether Pulsatile or Pulseless, with Counterpulsation as Technique for Myocardial Augmentation

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MECHANICAL SUPPORT for clinical heart failure without thoracotomy was first reported in 1955[1] and was first reported with long-term success in 1957.[2] Several recent comparative studies summarize work on mechanical cardiac assistance.[3-8] Reports include several methods to reduce cardiac work:

1. Veno-arterial pumping with or without oxygenation.[3, 4, 9, 10]
2. Left heart bypass with or without thoracotomy.[11-14]
3. Arterial counterpulsation, also termed postsystolic augmentation, and diastolic augmentation.[15-25]
4. External counterpulsation.[26-28]

We have elected to avoid the complications associated with prolonged use of an oxygenator[1, 2, 5, 29] and with thoracotomy or laparotomy.

We have compared the effect of left heart bypass (both pulseless and with synchronized pulsation) with that of arterial counterpulsation in terms of left ventricular work as measured by left ventricular pressure-time product and in the self same preparation.

Methods

After a series of exploratory experiments in which techniques were perfected, 11 mongrel dogs (19 to 27 kg) were anesthetized with intravenously administered pentobarbital (30 mg/kg), supplemented as needed. Spontaneous respiration through an endotracheal tube was permitted. Electrocardiographic leads were fed simultaneously into both a Cordis Cardiac Programmer and a Sanborn polychannel recorder. Clean nonsterile technique was employed.

Aortic pressure was recorded via a catheter placed in the aortic arch from the right carotid artery. Left ventricular pressure was monitored via a catheter placed into the left ventricle by way of the left carotid artery. On the same record, time of onset and duration of imposed pulsatile component in relation to the QRS complex were recorded, either electrically from the programmer or pneumatically from the pulsating chamber around the external ventricle (see below).

The technique of left heart bypass differs from that previously described.[30] Here, the human 6-mm Senning cannula* is passed down the right external jugular vein of the recumbent dog, the limbus of the fossa ovalis is "palpated" with the tip at the level of the midportion of the sternum, and puncture is made dorso-laterally without use of fluoroscopic control or the cutting tip.

Blood flows through the bypass circuit via the left atrial cannula, a heat exchanger (temperature monitored from the rectum), a Senning flowmeter, a siphon chamber (which protects the left atrium from the pulsation of the roller pump), a roller pump, the pulsating chamber, and bilateral femoral arterial cannulae (fig. 1). Closed side connections (not shown) permit addition or removal of blood without risk of air embolism.

In the pulsating chamber blood flows through a valveless 110-ml chamber made of a segment of 1.125-mm thick polyvinyl tubing (fig. 2). This lies in a rigid, air-over-saline compression

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Supported by the U. S. Public Health Service under Grant No. 2 R01 HE07028-05, "Surgical Approach to Acute Coronary Thrombosis."

*Manufactured by Stille-Werner, Stockholm; available in U.S.A. from Ohio Chemical Company, Madison, Wisconsin.

casing, and the chamber accomplishes ejection of blood by overlying air pressure at 600 mm Hg triggered by the cardiac programmer through a ¾ inch solenoid valve.

The pulsating chamber is immediately adjacent to the femoral artery cannulae. This minimized the inertial effect of the contained blood but requires that the saline level in the rigid casing surrounding it be 10 cm above the level of the left atrium.

Optimal delay (av. 0.1 sec), duration (av. 0.13 sec), and air pressure (600 mm Hg) were determined by preliminary studies in other dogs to reduce maximally the end-diastolic aortic pressure and left ventricular pressure-time product per minute (PTP), a variant of Sarnoff's tension-time index (TTI).[31] These adjustments were reconfirmed in each of the experiments here reported.

Ejection of blood from the pulsating chamber occurs only into the dog, for backflow is prevented either by the roller pump while on bypass or by a clamp adjacent to the pulsating chamber when it is used for counterpulsation without bypass. The possibility that failure of full occlusion by the roller pump or elasticity of the connecting tubing might permit some backflow during bypass has been evaluated in each experiment by electively routing the blood from the pump to the pulsating chamber through a one-way valve immediately adjacent to the pulsating chamber (fig. 1).

The indocyanine-green dilution method[32] is used for cardiac output determinations, with injection into the right ventricle and withdrawal from the aortic arch.

The previously sterilized pump circuit is primed with 500 ml of aseptically drawn, heparinized

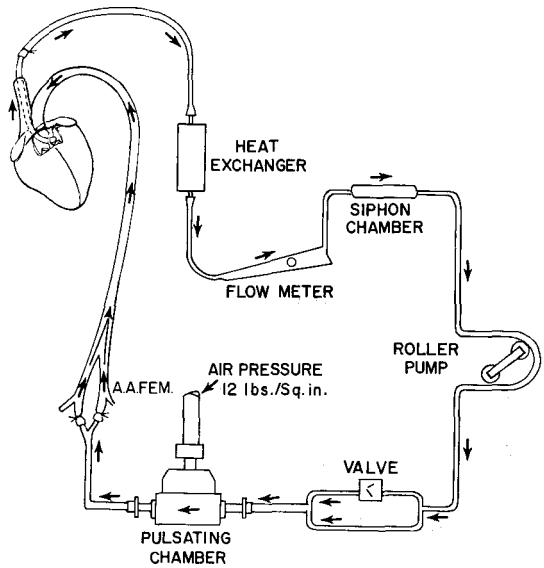

Figure 1

Bypass circuit.

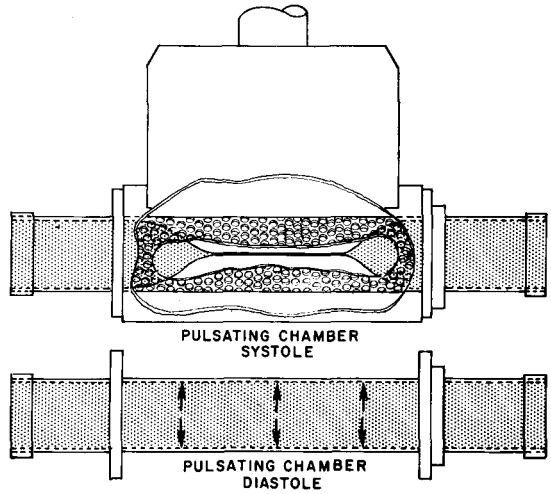

Figure 2

Pulsating chamber.

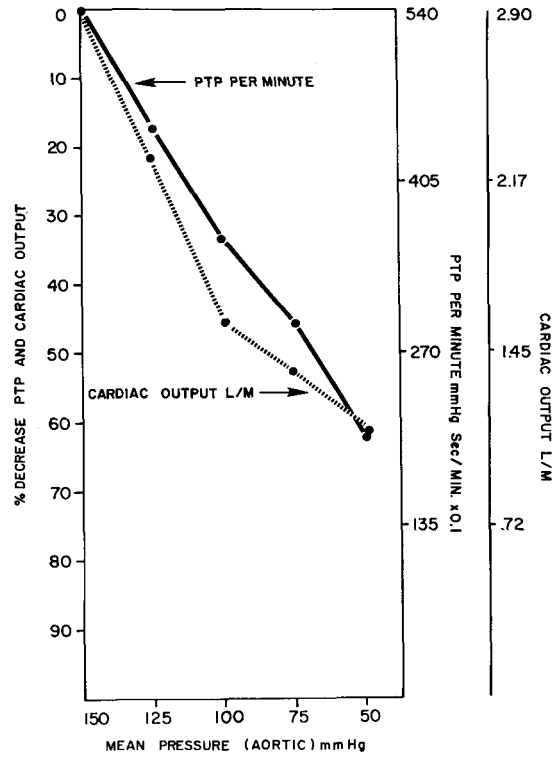

Figure 3

Changes in control values of pressure-time product/min and cardiac output with changes in mean aortic pressure.

Table 1

Pressure Time Product with and without Myocardial Assist

150				125				100				75				50			
Control I Control II	R	P	CPS	Control I Control II	R	P	CPS	Control I Control II	R	P	CPS	Control I Control II	R	P	CPS	Control I Control II	R	P	CPS
444				336				288				248				182			
447	416	331		359	312	263	317	310	226	214	274	265	191	153	224	181	47	78	162
410				409				353											
420	301	334	362	390	332	248		325	269	249	308	‡							
*				470				342				222				153			
				467	106	77	353	313	26	64	212	223	52	46	186	178	76	53	130
*				524				420				344				243			
				528	495	505	547	404	304	266	336	334	257	188	274	235	183	138	193
563				464				397				310				235			
555	521	446	462	466	432	330	383	372	211	121	288	315	81	125	283	338	193	162	188
540				389				344				303				178†			
504	502	366	429	392	321	233	313	318	233	218	243	273	296	188	226	250	130	136	252
452				387				308				232†				250†			
501	347	275	415	403	171	252	346	285	201	127	266	258		§		382		§	
626				517	432	338	390	402				302				242			
627	574	462	490	519				373	342	232	319	301	249	168	232	232	117	123	189
560				427				405				334				233			
558	482	455	462	427	368	364	400	450	134	240	361	349	66	88	266	247	59	70	181
618¶				462				354				355				191			
560	547			455	423			347	243			355	112			178	82		
584				565				400†				257				173			
600	564	617	624	598	517	431	504	326	308	249	304	233	209	171	197	169	145	125	163

PTP/min (mm Hq sec/min × 0.1)

Control I—preliminary control.
Control II—control following assist.
R—pulseless flow } left heart bypass.
P—pulsatile flow }
CPS—counterpulsation.

*Animals blood pressure could not be maintained at this level.
†Sequence eliminated (controls not reproducible within 5% of the mean).
‡Animal fibrillated.
§Malfunctioning recorder.
¶No compressed air available.

Table 2

Comparison of Aortic Tension Time Index (TTI) with Ventricular Pressure Time Products (PTP)

Exp. no.	Mean blood pressure (mm Hg)	Ventricular PTP (mm Hg sec/min × 0.1) Control I / Control II	CPS	% Change from control	Aortic TTI (mm Hg sec/min × 0.1) Control I / Control II	CPS	% Change from control
1	125	336 / 359	317	−8.9	228 / 242	219	−6.8
3	125	470 / 467	353	−24.6	507 / 495	336	−32.9
4	125	524 / 528	547	+4.0	348 / 315	342	+3.0
5	125	464 / 466	383	−17.6	438 / 383	328	−20.0
6	125	389 / 392	313	−19.7	413 / 426	308	−26.7
7	125	387 / 403	346	−12.4	338 / 363	288	−17.7
8	125	517 / 519	390	−24.7	371 / 378	279	−25.4
9	125	427 / 427	400	−6.3	371 / 379	376	+0.3
11	125	565 / 598	504	−13.4	455 / 422	402	−8.2

Control I—preceding control.
Control II—control following assist.

donor blood and 300 ml of 0.9% sodium chloride solution. The dog is heparinized with 4 mg/kg initially and 2 mg/kg every hour for the duration of the experiment.

At the start, partial bypass is utilized to provide thorough mixing of host blood and prime, while pulse, blood pressure, and electrocardiogram are observed. All 11 subjects in this report are those free from change at this stage. All studies reported here were performed with the mean blood pressure within 4 mm Hg of the control level, most within 2 mm Hg, the levels being adjusted only by addition or subtraction of blood from the circuit.

Each experiment consisted of a series of sequences, each in turn consisting of left heart bypass with pulseless flow, left heart bypass with pulsating return, left heart bypass with pulsating return through the one-way valve described above, and counterpulsation without bypass. Each sequence was preceded and followed by observations without bypass or counterpulsation (control). Each experiment consisted of such a series at 150 mm Hg, one at 125 mm Hg, and so on down in steps of 25 mm Hg to a final 50 mm Hg. Bypass was done at maximal flow rates.

The left ventricular PTP was measured with a compensating polar planimeter from the beginning rise to the terminal fall of left ventricular pressure, with atmospheric pressure as the baseline. This variant of Sarnoff's TTI was used because of the common disappearance of the left ventricular component of the aortic pressure tracing when bypass was in force.

Control values used in calculating results were the average of the two or more controls at any given mean pressure. When the control values differed by more than 10% (5% from the mean) the whole sequence was discarded. This occurred four times in a total of 50 sequences. The data were analyzed statistically by the difference-of-the-means test.[33]

Results

Determinations during control studies reveal a progressive decrease in cardiac output as aortic pressure is lowered (fig. 3). This parallels the reduction in left ventricular PTP as the mean pressure decreases. The

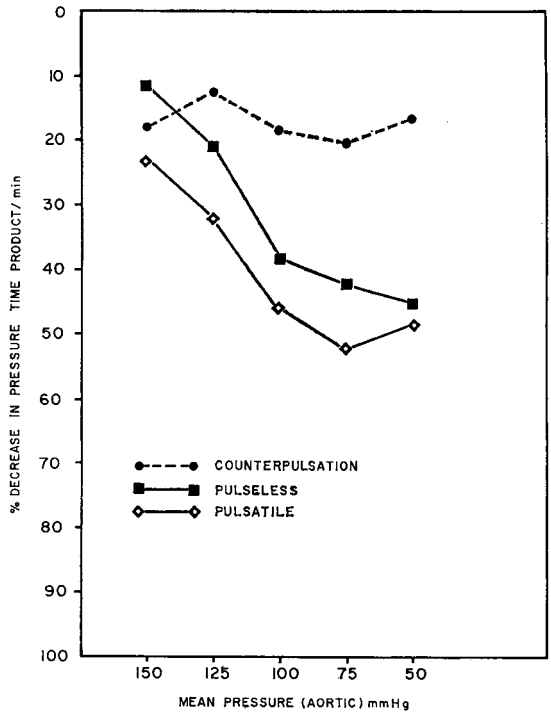

Figure 4

Reduction of pressure-time product with left heart bypass and counterpulsation.

values in figure 3 represent the comparison of controls at lower mean pressures with controls at 150 mm Hg.

Comparison of the values of PTP of controls at progressively lower mean aortic pressure levels reveals a decrease in the PTP resulting solely from the decrease in mean aortic pressure (fig. 3). It is for this reason that the mean blood pressure was held within 4 mm Hg of the control by addition or removal of blood.

All forms of support tested reduced the PTP below controls at the same aortic mean pressures. All such reductions were statistically significant ($P < 0.01$). At all aortic mean pressures below 150 mm Hg, pulseless left heart bypass reduced the PTP more than simple counterpulsation. At mean aortic pressures of 50 mm Hg, 75 mm Hg, and 100 mm Hg these differences were statistically significant ($P > 0.05$). At 125 mm Hg, pulseless bypass produced a decrease in PTP 8.7% (39 of 453 mm Hg sec/min) greater than that produced by simple counterpulsation. However, this difference was not statistically significant ($P < 0.05$). At all aortic mean pressures below 150 mm Hg, both forms of pulsatile left heart bypass reduced left ventricular PTP statistically significantly more than did simple counterpulsation ($P < 0.01$).

Inasmuch as the data on pulsatile bypass with a one-way valve were essentially identical to those without the valve, they are omitted from this report.

The volume of blood moved with each stroke of counterpulsation was 15 to 20 ml, whereas the volume moved with each pulsation during left heart bypass was 40 to 45 ml. Flow rates with left heart bypass at 150 mm Hg mean aortic pressure ranged between 67 and 110 ml/kg/min. There was a 7 to 12% decrease in flow rate with each 25 mm Hg decrease in mean aortic pressure.

With simple counterpulsation the decrease in PTP below controls at the same aortic mean pressure was between 12.8% (58 of 453 mm Hg sec/min) and 20.1% (58 of 288 mm Hg sec/min) regardless of the mean aortic pressures.

Although there appeared to be a tendency for pulsatile forms of left heart bypass to decrease the PTP more than pulseless forms, this could not be proved statistically. The addition of the valve between the pulsating chamber and the roller pump had no effect.

At lower-than-normal mean aortic pressures, i.e., below 125 mm Hg, the average reduction in PTP with the various forms of left heart bypass ranged between 38.2% (136 of 355 mm Hg sec/min) and 50.9% (155 of 296 mm Hg sec/min) of control observations at identical mean aortic pressures although individual observations revealed reductions as great as 92.2% (302 of 328 mm Hg sec/min) (table 1).

The results of individual experiments are tabulated in table 1, and the averages are shown graphically in figure 4. Representative tracings are shown in figures 5, 6, and 7.

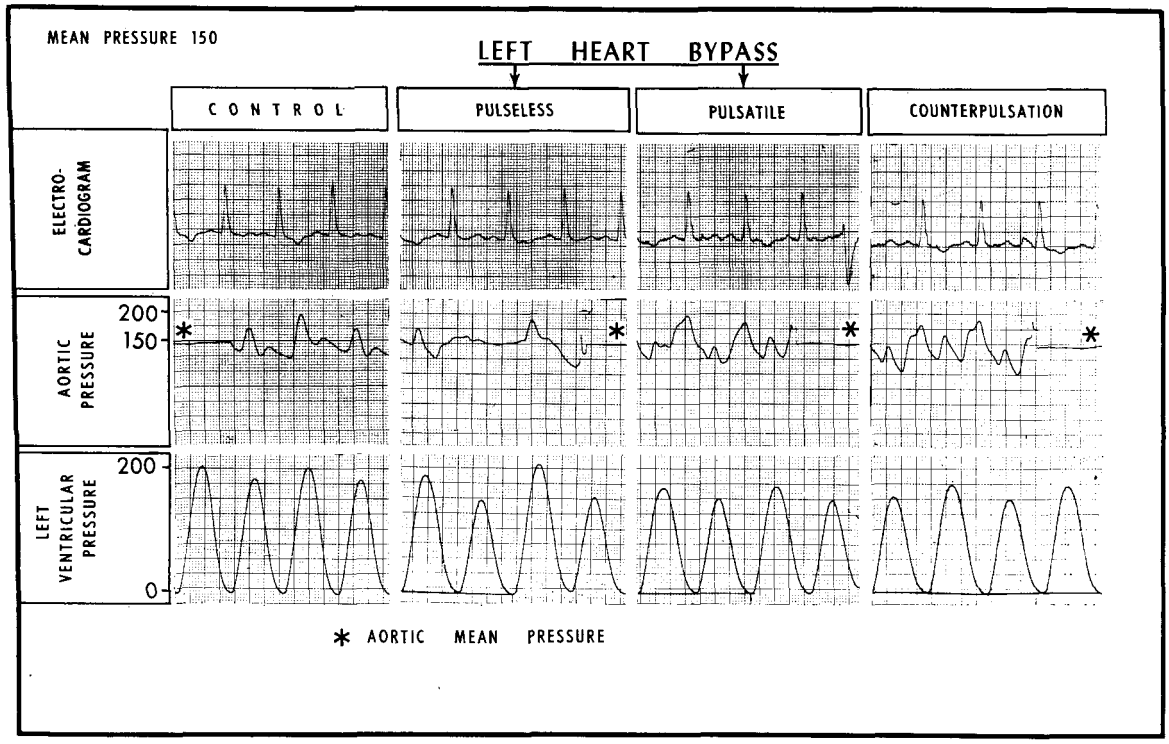

Figure 5

Representative tracings at 150 mm Hg mean aortic pressure.

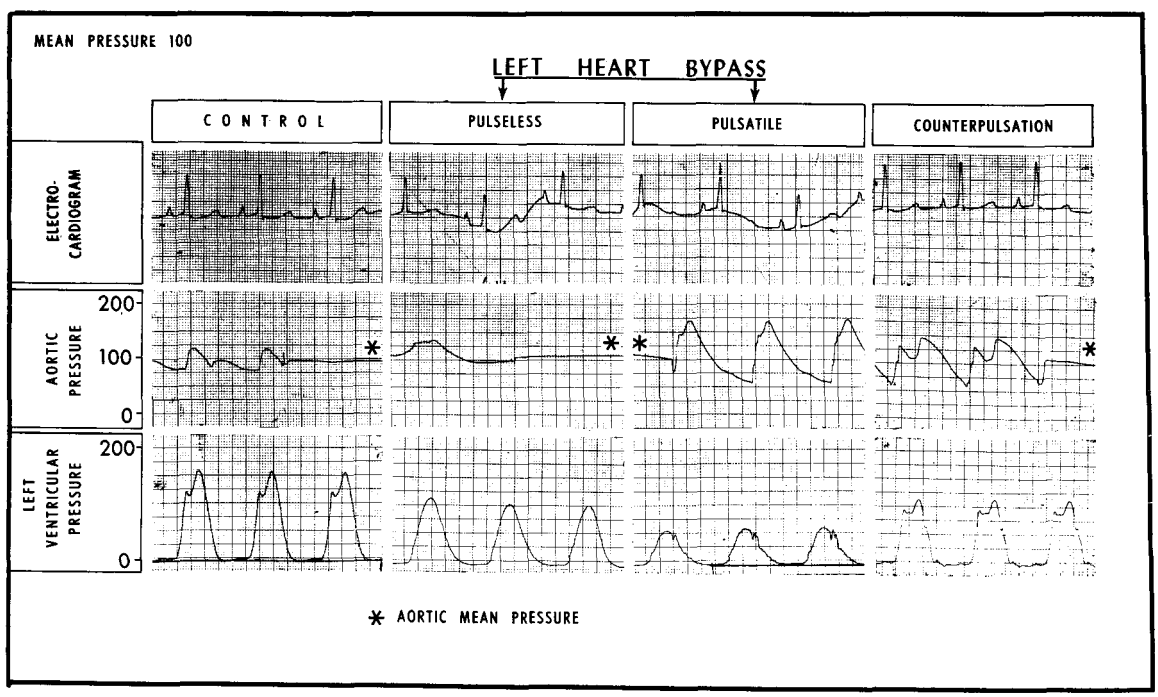

Figure 6

Representative tracings at 100 mm Hg mean aortic pressure.

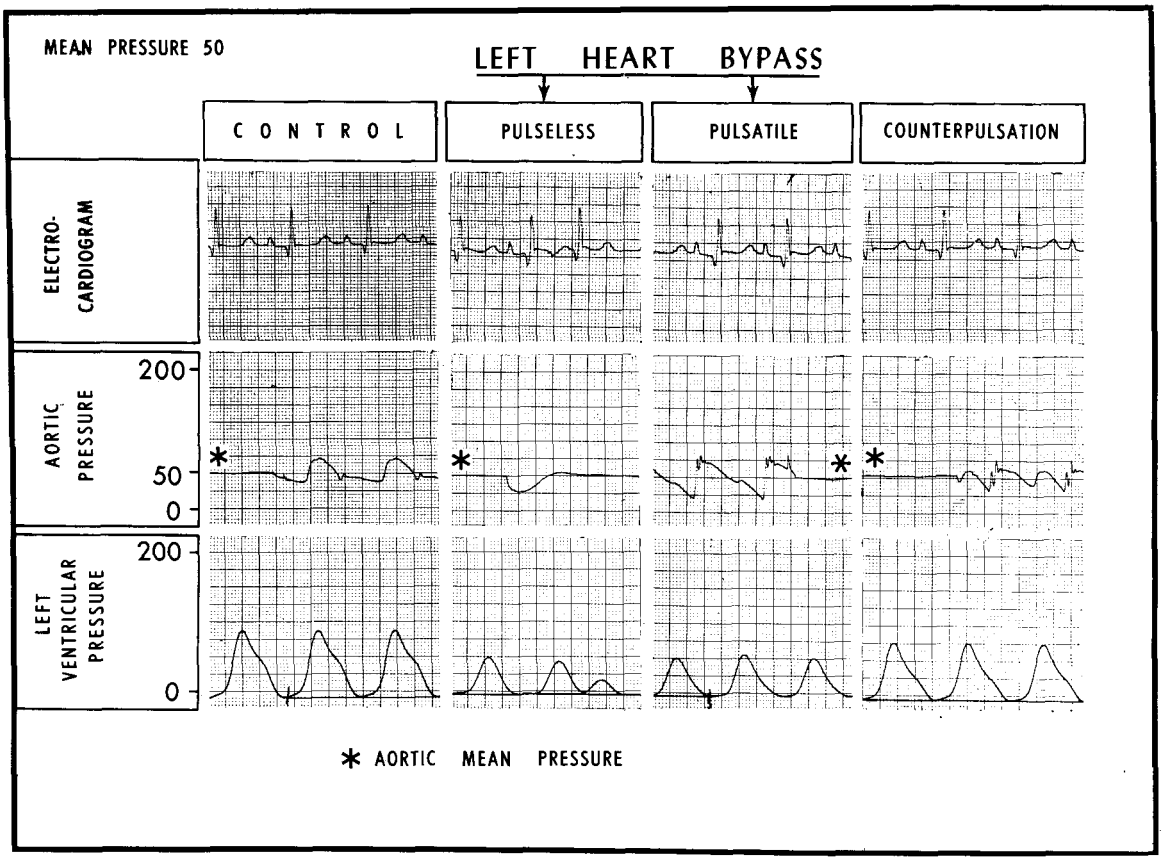

Figure 7

Representative tracings at 50 mm Hg mean aortic pressure.

Although aortic TTI ceases to have meaning on near total left heart bypass, TTI determinations were made on the counterpulsation experiments at 125 mm Hg mean pressure for comparison with simultaneous measurements of left ventricular PTP. The findings are shown in table 2. The correlation is consistent.

Discussion

Our results are based on a modification of the tension-time index as described by Sarnoff,[31] who showed a relationship between myocardial oxygen consumption and TTI. We believe that the entire area under the left ventricular curve reflects the pressure generated by the left ventricle; and, hence, the total work of this part of the heart. The artificial movement of blood by various pumping systems may produce changes in the characteristics of the aortic pressure curve that could invalidate utilization of this parameter in determination of left ventricular work.

To evaluate properly the effects of various pumping systems in reducing the TTI or the PTP and, hence, the myocardial oxygen utilization and myocardial work, we have demonstrated that it is essential to maintain aortic mean pressure at constant levels during control studies and periods of circulatory assist. This permits an objective comparison by separation of extraneous factors, such as the effects of hypovolemia and the changes in peripheral resistance produced by various systems of circulatory assist.

Other investigators[16, 19, 20] have failed to emphasize the need for keeping mean pressure constant, although Baird et al.[12] and Shenk

et al.[24] have made some mention of the importance and effect of mean pressure.

Our data reveal that left heart bypass is most efficient at mean aortic pressures between 75 and 100 mm Hg. Our failure to produce decreases of similar magnitude in PTP at higher mean pressures (150 and 125 mm Hg) may reflect our inability to achieve complete bypass at those pressures. This may be secondary either to incomplete sumping of the left atrium or to the Thebesian blood flow to the left ventricle, or both. Studies by Dennis et al.[34] have shown that partial left heart bypass produces a decrease in the myocardial oxygen consumption without a decrease in the PTP, and that the PTP decreases only as complete bypass is approached. Failure of reduction at higher mean aortic pressures equal to that seen during hypotension in the reported experiments does not necessarily preclude substantial reduction in oxygen consumption or myocardial work.[34]

Several questions remain to be answered relating to organ perfusion, coronary blood flow, and changes in peripheral resistance. Davidson and Leighninger[35] have shown that reduction of aortic pressure results in a decrease in back bleeding from the distal end of a divided coronary artery and therefore probably a decrease in blood flow through collateral vessels. They suggest that high perfusion pressures should be maintained in coronary arteries to ensure adequate myocardial oxygenation.

Considerable interest has recently been shown in evaluating the more physiological pulsatile type of flow.[36] Our experiments were of a short-term nature and did not reveal a significant difference between pulseless and pulsatile flow; but, as seen in figure 4, pulsatile flow showed a tendency to decrease the PTP to a greater extent. Wesolowski[37] showed no significant physiological difference between pulseless and pulsatile flow at rates of 130 cc/kg/min. However, other investigators[29, 38] have demonstrated more metabolic acidosis, weight gain (edema), splanchnic pooling, capillary stasis and opening of A-V shunts with pulseless flows of less than 100 cc/kg/min. Nakayama et al.[39] showed a decrease in perfusion of the heart and kidneys during nonpulsatile as compared with pulsatile systemic flow. Dalton et al.[40] have shown that pulsatile flow has advantages over pulseless flow with total cardiopulmonary bypass, but they were unable to demonstrate similar benefits with left heart bypass only. Parsons and McMaster[41] demonstrated a decrease in lymph flow in rabbits with pulseless perfusion. More clarification of the role of the pulse is required.

Our studies have shown that any form of left heart bypass decreases the PTP more than counterpulsation as achieved by our apparatus, especially at mean pressures of 125, 100, and 75 mm Hg. With counterpulsation the entire cardiac output must pass through the left ventricle, whereas with left heart bypass a significant amount of the cardiac output is diverted from the left atrium into the bypass circuit. Our results suggest once again that cardiac output as such plays a role in determination of the work of the heart as expressed by PTP. This may be tied to demonstration of the shortening of left ventricular end-diastolic fiber length produced by partial left heart bypass.[42]

Our system of counterpulsation does not have an active aspiration phase for withdrawal of blood from the aorta. Our system employs only a gradient from arterial pressure to a level 10 cm above the left atrium. However, our results are comparable to other studies using an active withdrawal phase (Davol pump) with cannulation of one or more peripheral vessels.[21, 23, 24] Our system does not produce the greater decreases in TTI reported by laboratories that use cannulation of the distal abdominal aorta for the assist site.[19, 20, 22] That we record lesser reductions in PTP than others have reported in aortic TTI's suggests careful analysis of the effect of the very pressure change imposed by the assist methods employed. Attempts to analyze the aortic pressure tracings in our experiments to calculate TTI values while counterpulsation is in force are fraught with indecision as to the precise point of aortic valve

closure. Employment of ventricular PTP appears to us to be a far more reliable index of true effect.

There is an apparent need for a readily applicable system of myocardial augmentation in clinical situations. We believe that the ideal system should have certain characteristics, specifically (1) the system should utilize the patients own lungs as oxygenators to avoid the complications inherent in the use of artificial oxygenators and (2) the system should impose a minimal additional tax on the critically ill patient. This would preclude utilization of a system that requires laparotomy or thoracotomy.

Clinical application of left heart bypass without thoracotomy under local anesthesia has been demonstrated to be feasible.[43] Further studies are required to evaluate pulseless versus pulsatile flow; the importance of mean pressure as a reflection of peripheral resistance, organ perfusion, and cardiac output; and oxygen uptake by the left ventricle with the reported patterns of support.

Summary and Conclusions

Determinations of left ventricular pressure-time product (PTP) per minute during left heart bypass compared with counterpulsation in the same dog have shown a significantly greater reduction of PTP with all forms of left heart bypass.

Precise control of mean aortic pressure has again[34] been proved essential to evaluation of methods of myocardial assist.

Since some forms of assist alter the nature of the aortic pressure tracing or even obliterate the left ventricular component of that tracing (as left heart bypass) and since the timing of the beginning and end of systole for use of aortic pressure in calculating tension-time index (TTI) cannot well be accomplished without the left ventricular pressure tracing, direct use of the left ventricular PTP is a more usable index of effectiveness of the several methods of assist than TTI.

Left heart bypass is more effective in lowering PTP at mean pressures of 100 and 75 mm Hg than at mean pressures of 150 and 125 mm Hg.

Further studies are needed.

References

1. Newman, M. H., Stuckey, J. H., Levowitz, B. S., Young, L. A., Dennis, C., Gorayeb, E. H., Zuhdi, M., Karlson, K. E., Adler, S., and Gliedman, M.: Complete and partial perfusion of animal and human subjects with the pump oxygenator. Surgery **38**: 30, 1955.
2. Stuckey, J. H., Newman, M. M., Dennis, C., Berg, E. H., Goodman, S. E., Fries, C. C., Karlson, K. E., Blumenfeld, M., Weitzner, S. W., Binder, L. S., and Winston, A.: The use of the heart-lung machine in selected cases of acute myocardial infarction. Surgical Forum **8**: 342, 1957.
3. Salisbury, P. F., Cross, C. E., Risben, P. A., and Lewin, R. J.: Comparison of two types of mechanical assistance in experimental heart failure. Circulation Research **8**: 431, 1960.
4. Salisbury, P. F.: Mechanical assistance to the circulation in heart failure. Bibl Haemat **13**: 56, 1962.
5. Connolly, J. E.: An appraisal of methods to support the circulation mechanically in acute heart failure. J Cardiov Surg **5**: 257, 1964.
6. Ellis, P. R., Lee, C., Wong, S. H., DelRosario, V. C., Hyland, J. W., and Prater, G.: Assisted circulation in the treatment of experimental heart failure. Arch Surg **90**: 879, 1965.
7. Malette, W. G., and Eiseman, B.: Mechanical aid to the failing heart. A review. Amer Surgeon **31**: 406, 1965.
8. Bernstein, E. F., Castaneda, A. R., Blackshear, P. L., and Varco, R. L.: Prolonged mechanical circulatory support: Analysis of certain physical and physiologic considerations. Surgery **57**: 103, 1965.
9. Connolly, J. E., Bacaner, M. B., Bruns, D. L., Lowenstein, J. M., and Storli, E.: Mechanical support of the circulation in acute heart failure. Surgery **44**: 255, 1958.
10. Kuhn, L. A., Gruber, F. L., Frankel, A., and Kupfer, S.: Hemodynamic effects of the extracorporeal circulation in closed chest normal dogs and in those with myocardial infarctions. Surgical Forum **10**: 616, 1960.
11. Hall, D. P., Moreno, J. P., Dennis, C., and Senning, A.: Left heart bypass as a means of support for a failing heart. Bull Soc Int Chir **21**: 607, 1962.
12. Baird, R. J., Labrosse, C. J., Lajos, T. Z., and Thomas, G. W.: Effects of selective bypass of the left ventricle. Circulation **27**: 835, 1963.

13. DENNIS, C., GROSZ, C., WESOLOWSKI, S. A., AND CHIU, C-J.: External circulatory support in acute heart failure. J Cardiov Surg **5**: 626, 1964.
14. DENNIS, C., SENNING, A., HALL, D. P., MORENO, J., CARLENS, E., WESOLOWSKI, S. A., GROSZ, C., AND CHIU, C-J.: Background for use of left heart bypass in treatment for acute left heart failure. Heart Bull **13**: 109, 1964.
15. CLAUSS, R. H., BIRTWELL, W. C., ALBERTAL, G., LUNZER, S., TAYLOR, W. T., AND FOSBERG, A. M.: Assisted circulation. I. Arterial counterpulsator. J Thorac Cardiov Surg **41**: 447, 1961.
16. LEFEMINE, A. A., LOW, H. B. C., COHEN, M. L., AND HARKEN, D. E.: Assisted circulation. II. Effect of heart rate on synchronized arterial counterpulsation. Amer Heart J **64**: 779, 1962.
17. LEFEMINE, A. A., LOW, H. B. C., COHEN, M. L., LUNZER, S., AND HARKEN, D. E.: Assisted circulation. III. Effect of synchronized arterial counterpulsation on myocardial oxygen consumption and coronary flow. Amer Heart J **64**: 789, 1962.
18. WATKINS, D. H., DUCHESNE, E. R., AND POLLOCK, B. E.: Coordinated postsystolic myocardial augmentation combined with systolic neutralization; development and clinical application to the failing heart. J Thorac Cardiov Surg **43**: 1, 1962.
19. BIRTWELL, W. C., SOROFF, H. S., WALL, M., LEVINE, H. J., AND DETERLING, R. A., JR.: Assisted circulation. I. An improved method for counterpulsation. ASAIO **8**: 35, 1962.
20. SOROFF, H. S., LEVINE, H. J., SACHS, B. F., BIRTWELL, W. C., AND DETERLING, R. A., Jr.: Assisted circulation: Effects of counterpulsation on left ventricular oxygen consumption and hemodynamics. Circulation **27**: 722, 1963.
21. CRONIN, R. F. P., AND CALATAYUD, J. B.: Hemodynamic effects of synchronous arterio-arterial pumping after experimental myocardial infarction. Amer J Cardiol **11**: 768, 1963.
22. SACHS, B. F., SOROFF, H. S., BIRTWELL, W. C., LEVINE, H. J., AND DETERLING, R. A., JR.: Hemodynamic effects of counterpulsation: Evaluation of proper and improper phasing on left ventricular oxygen consumption. Tufts Folia Med **9**: 17, 1963.
23. CALLAHAN, P. B., AND WATKINS, D. H.: A new technique for assisting the damaged heart; post-systolic myocardial augmentation. Clin Med **71**: 1329, 1964.
24. SHENK, W. G., JR., DELIN, N. A., CAMP, F. A., MCDONALD, K. E., AND POLLOCK, L.: Assisted circulation: An experimental evaluation of counterpulsation and left ventricular bypass. Arch Surg **88**: 327, 1964.
25. GOLDFARB, D., MCGINNIS, G. E., AND BALLINGER, W. F. II.: An improved system for diastolic augmentation. ASAIO **11**: 31, 1965.
26. DENNIS, C., MORENO, J. R., HALL, D. P., GROSZ, C., ROSS, S. M., WESLOWSKI, S. A., AND SENNING, A.: Studies on external counterpulsation as a potential measure for acute left heart failure. ASAIO **9**: 186, 1963.
27. BIRTWELL, W. C., SOROFF, H. S., SACHS, B. F., LEVINE, H. J., AND DETERLING, R. A., JR.: Assisted circulation: V. The use of the lungs as a pump. A method for assisting pulmonary blood flow by varying airway pressure synchronously with the EKG. ASAIO **9**: 192, 1963.
28. BIRTWELL, W. C., GIRON, F., SOROFF, H., RUIZ, U., COLLINS, J., AND DETERLING, R.: Support of the systemic circulation and left ventricular assist by synchronous pulsation of extra-mural pressure. ASAIO **11**: 43, 1965.
29. CREECH, O., JR., AND PEARCE, G. W.: Physiologic considerations in cardiopulmonary bypass. Surg Clin N Amer **45**: 289, 1965.
30. DENNIS, C., HALL, D. P., MORENO, J. A., AND SENNING, A.: Left atrial cannulation without thoracotomy for total left heart bypass. Acta Chir Scand **123**: 267, 1962.
31. SARNOFF, S. J., BRAUNWALD, E., WELCH, G. M., JR., STARNSBY, W. N., AND MACRUZ, R.: Hemodynamic determinants of the oxygen consumption of the heart with special reference to the tension-time index. Amer J Physiol **192**: 148, 1958.
32. FOX, I. J., BROOKER, L. Q. S., HESELTINE, D. W., AND WOOD, E. H.: A tricarbocyanine dye for continuous recording of dilution curves in whole blood independent of variations in blood oxygen saturation. Proc Mayo Clin **32**: 478, 1957.
33. BANCROFT, H.: Introduction to Biostatistics. New York, Paul B. Hoeber, Inc., 1957, p. 74.
34. DENNIS, C., HALL, D. P., MORENO, J. R., AND SENNING, A.: Reduction of the oxygen utilization of the heart by left heart bypass. Circulation Research **10**: 298, 1962.
35. DAVIDSON, A. I. G., AND LEIGHNINGER, D. S.: Collateral flow to the heart at different aortic perfusion pressures using left heart bypass. Ann Surg **162**: 48, 1965.
36. MANDELBAUM, I., AND BURNS, W. H.: Pulsatile and non-pulsatile flow. JAMA **191**: 657, 1965.
37. WESOLOWSKI, S. A.: The role of the pulse in maintenance of the systemic pressure during heart-lung bypass. ASAIO **1**: 84, 1955.
38. OGATA, T., IDA, Y., NOMOYAMA, A., TAKIDA, J., AND SASAKI, H.: A comparative study of pulsatile and non-pulsatile flow in extra-corporeal circulation. Arch Jap Chir **29**: 59, 1960.

39. NAKAYAMA, K., TAMIYA, T., YAMAMOTO, K., IZUMI, T., AKIMOTO, S., IIMORI, T., ODAKA, M., AND YAZAWA, C.: High amplitude pulsatile pump in extracorporeal circulation with particular reference to hemodynamics. Surgery **54**: 798, 1963.
40. DALTON, M. L., JR., MCCARTY, R. T., WOODWARD, K. E., AND BORILA, T. G: The army artificial heart pump II. Comparison of pulsatile and non-pulsatile flow. Surgery **58**: 840, 1965.
41. PARSONS, R. J., AND MCMASTER, P. D.: The effect of pulse upon the formation and flow of lymph. J Exper Med **68**: 353, 1938.
42. CHIU, C-J., DENNIS, C., AND HARRIS, B.: Response of myocardial fiber length to left-heart bypass. Abstract. Circulation **34** (Suppl. 3): III-74, 1966.
43. DENNIS, C., CARLENS, E., SENNING, A., HALL, D. P., MORENO, J. P., CAPPELLETTI, R. R., AND WESOLOWSKI, S. A.: Clinical use of a cannula for left heart bypass without thoracotomy. Ann Surg **156**: 623, 1962.